Evaluation of the Efficacy of Propofol-Magnesium Sulfate Combination for Sedation in Paediatric Magnetic Resonance Imaging of Brain.- a Randomized Controlled Trial.

Prashant Atmaram Lomate[1], Ganesh Mallappa Kumbhar[1*], Jyotsna Satish Paranjpe[1]

Bharati Vidyapeeth (deemed to be university) medical college and hospital, Sangli, India.

Background and Aims: The key to successful sedation for pediatric magnetic resonance imaging (MRI) is to keep the child completely immobile while ensuring rapid recovery. We compared the efficacy of propofol-midazolam and propofol-magnesium sulfate sedation for MRI of the brain in the paediatric population. **Methods**: Total 60 paediatric patients, aged 1 to 8 years awaiting for MRI brain were randomly allocated into two groups. Group I patients received midazolam 0.05mg/kg and Group II patients received magnesium sulfate 30 mg/kg infusion in the preinduction room. In the MRI room all patients were sedated with 1-2 mg/kg bolus and 100 ug/kg/min infusion of propofol. The two groups were compared for sedation characteristics like discharge time, total number of additional propofol boluses, agitation scores, haemodynamic parameters and adverse events. Fisher exact test was used for all quantitative data. **Results**: Induction time, scan quality, requirement of additional propofol boluses and awakening time were comparable for the groups (P>0.05). There was no statistically significant incidence of airway instrumentation between both groups (p=0.14).). Heart rate remained on lower normal side, 20 minutes after induction in Group II (P<0.00). Incidence of emergence agitation was significantly lower in Group II (P<0.01). The discharge time was shorter in Group II (41.03 ± 8.39 min versus 32.83 ± 5.97 min;P<0.001). **Conclusion**: Propofol-magnesium sulfate sedation is a better alternative to propofol-midazolam combination for paediatric brain MRI, as it provides a shorter discharge time and a lower incidence of emergence agitation.

Key words: Agitation, magnesium sulfate, magnetic resonance imaging, midazolam, propofol.

Introduction

Paediatric patients with epilepsy or cerebral palsy require diagnostic magnetic resonance imaging (MRI) of the brain. It requires motionless child to acquire good quality images. An ideal sedative should provide rapid onset and rapid recovery.[1]

*Correspondence: Ganesh Mallappa Kumbhar
E mail: drganeshkumbhar@gmail.com
https://orcid.org/0000-0002-1480-7724

Received: 15/06/2021
Accepted: 30/03/2022

DOI: https://doi.org/10.4038/slja.v30i1.8873

Propofol is the most used drug due to its rapid onset time and short recovery time.[2] However loss of airway patency is common with its use. Midazolam, a benzodiazepine derivative has synergistic effect with propofol.[3]

Magnesium sulfate, a N-methyl-D-aspartate (NMDA) receptor antagonist has sedative, analgesic, bronchodilator, anticonvulsant and anti-agitation properties.[4] It maintains the airway tone and hence decreases chances of airway collapsibility.

A randomized trial was conducted to compare the sedation, complications, recover and side effect profile of propofol-midazolam and propofol-magnesium sulfate sedative regimes for MRI in children.

Methods

This prospective randomized single blind study was carried out in 60 ASA grade I and II paediatric patients of either sex, aged 1 to 8 years admitted for elective magnetic resonance imaging (MRI) of brain. This study was carried out in a tertiary care unit of India where there is no MRI compatible anaesthesia machine and monitors for blood pressure, bispectral index (BIS) and end tidal carbondioxide ($EtCO_2$) monitoring available to date. This study was conducted after obtaining hospital ethical committee approval and informed written consent from the parents. Patients having any severe cardiorespiratory and renal disease or known propofol allergy were excluded from the study. The confounding variables which may interfere with the study results such as patients having acute or chronic pain conditions, were also excluded from the study. The patients were randomly divided into two groups by a computer generated random list and allocation was done by a sealed envelope technique. The allocation was revealed to the anaesthesiologist who prepares the solutions for infusion. Thirty minutes before MRI, Group I patients received injection midazolam 0.05mg/kg as per routine institutional protocol and Group II patients received injection magnesium sulfate 30mg/kg, both diluted to 20cc with normal saline. The Anaesthesiologists involved in randomization and data collection, parents and radiologists were kept blinded to the study drug.

In the MRI room, patients were sedated with propofol 1 to 2 mg/kg given slowly till the University of Michigan Sedation Scale (UMSS) of 3 was achieved. Assessment of level of sedation was done by UMSS as, 0 = awake and alert, 1 = minimally sedated (responds to verbal conversation or sound), 2 = moderately sedated (arouses to light tactile stimuli), 3 = deeply sedated (arouses to deeper physical stimuli), 4 = unarousable to stimuli).[2] Propofol infusion was started at 100 ug/kg/min rate. Oxygen supplementation was given with a face mask and child was moved inside the MRI gantry. In case of involuntary movements, additional bolus of 0.5 mg/kg propofol was given.

In the MRI room, the induction time (time to achieve UMSS=3 after propofol bolus), number of additional propofol boluses, awakening time (time to achieve UMSS=1 after stopping of propofol infusion) and scan time (time from start of scan to its completion) were monitored. The HR, respiratory rate and SpO_2 were measured every five minutes. At the end of the scan, the radiologist was asked to grade the scan quality as, Excellent = no movement or scan artifacts; good = minor movement or scan artifacts; and poor = major movement causing scan pausing. The patients with sedation failure, who required co-administration of other sedo-analgesics were excluded from the analysis.

Bradycardia (HR less than 20% from baseline) was treated with injection atropine, agitation was treated with injection midazolam. Upper airway obstruction was managed by gently inserting smallest possible, lubricated, nasopharyngeal airway (NPA).[5] The NPA was attached to the Jackson Rees(JR) circuit, which was connected to the auxiliary oxygen outlet with the help of a long extension tube. Five to six litres of oxygen flow was started. This ensured unobstructed airway, adequate oxygenation and confirmation of adequacy of patient's respiratory efforts by observing reservoir bag movements. Number of patients requiring airway intervention with NPA were recorded. Post-anaesthesia agitation was detected by using WATCHA scale, as asleep=0; calm=1; crying but can be consoled =2; crying but cannot be consoled = 3; agitated and thrashing around = 4. Patients with scores three or more than three were considered as having agitation.[6] The discharge time (time to attain modified Aldrete score >9) was noted in the recovery room.

Sample size was calculated after doing a pilot study with 10 patients in each group. It showed a mean discharge time of 36.5 (±9.44) min in group I and 29.0 (±6.58) min in group II. With a 5% α level of significance and 90% power of the test, minimum

sample size calculated was 25 patients per group. Statistical analysis was done by using SPSS version 22 for Windows (IBM – Chicago). Categorical variables were analyzed using the Fisher's exact test. The unpaired t-test was applied to compare continuous variables of two independent groups. P < 0.05 was considered as statistically significant.

Results

Sixty patients were enrolled for the study, out of which 59 patients were analyzed, as one patient from group I was excluded from the analysis due to sedation failure. The two groups were statistically comparable with respect to the age (3.35±2.07 vs 3.0±1.72 yrs), weight (12.14±2.86 vs 12.47±3.17 kg), sex ratio and scan duration (33.97±4.89 min vs 34.5±4.79 min). The results regarding the induction time and the number of additional bolus doses of propofol required in two groups are summarized in Table 1. The scan quality was comparable between groups. It was excellent in 26 vs 27, good in 2 vs 2 and poor in 1 vs 1 patients [p<0.05]. The data on number of patients requiring airway manipulation, the incidence of apnoea, hypoxia, nausea and vomiting is shown in Table 2. One patient from group I developed bradypnoea which was successfully managed with assisted ventilation [Table 2]. The heart rate remained comparable in both groups five minutes after injection of study drugs and up to 15 minutes post-induction [P >0.05] [Figure 1]. But the heart rate levels from 20 to 45 minutes post-induction were on lower normal side in group II [P= 0.00][Figure 1]. However, only two patients from group II developed bradycardia, which was successfully managed with atropine, the difference being statistically insignificant [P=0.49] [Table 2]. The incidence of agitation was lower in group II than in group I. The difference was statistically significant for agitation scores 3 [P= 0.02] and 4 [P= 0.01] [Figure 2]. The awakening time was statistically comparable between two groups [Table 1]. The mean duration of discharge time was significantly shorter in group II than in group I [P < 0.00] [Table1].

***Figure 1** : Comparison of mean heart rate (HR- heart rate per minute).*

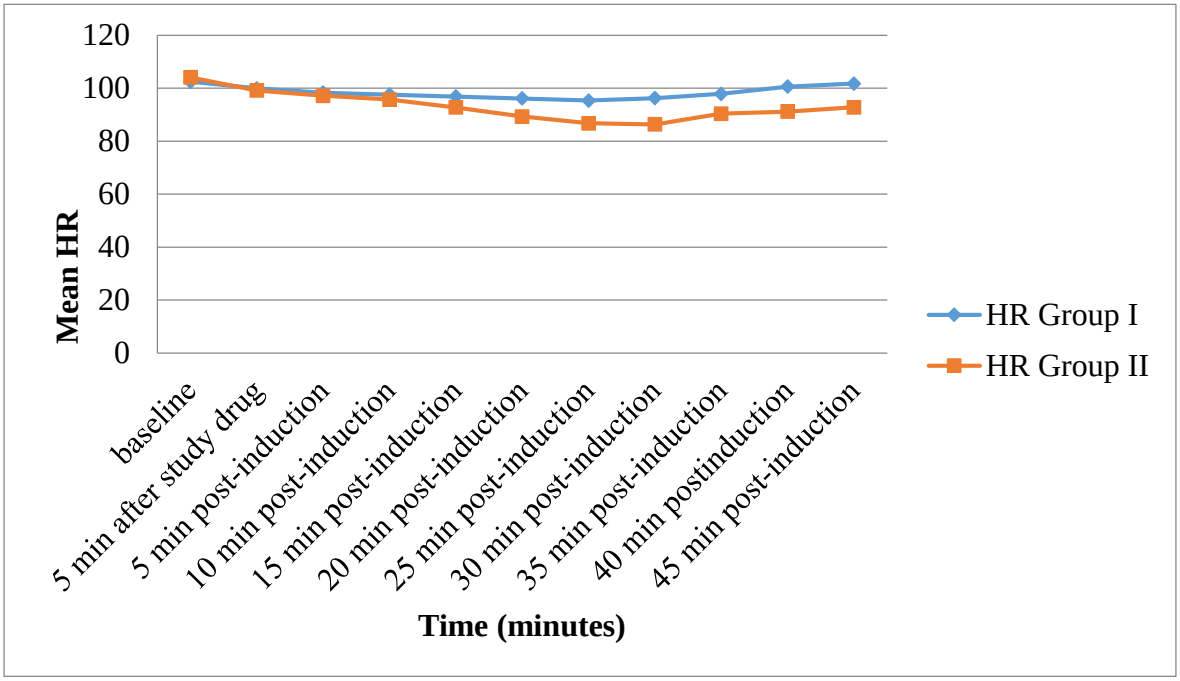

***Figure 2**: Comparison of agitation scores (WATCHA scale). Data presented as numbers*

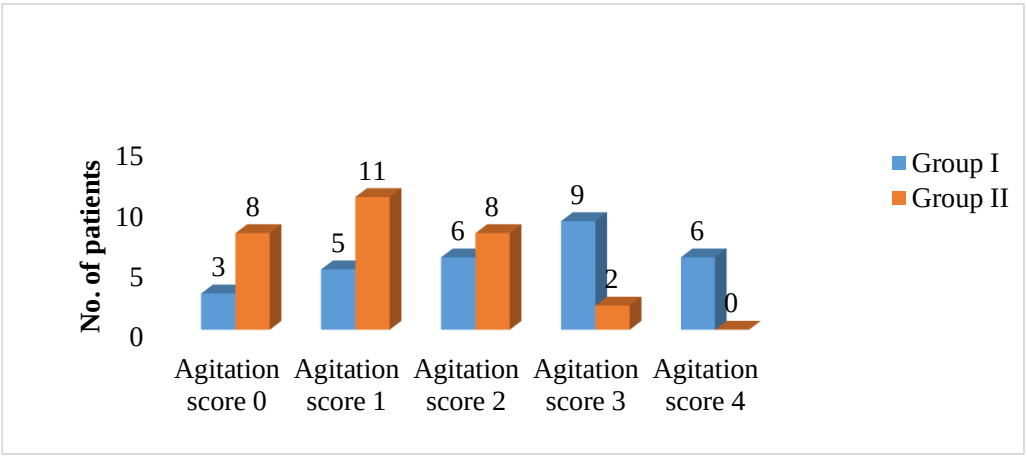

***Table 1**. Comparison of sedation characteristics*

Parameters	Group I (n=29) mean ± SD	Group II (n=30) mean ± SD	P value
0 propofol bolus. [n(%)]	20 (68.9)	24 (80.0)	0.38
1 propofol bolus. [n(%)]	4 (13.7)	2 (6.6)	0.42
2 propofol boluses. [n(%)]	4 (13.7)	3 (10.0)	0.71
3 propofol boluses. [n(%)]	1 (3.4)	1(3.3)	1
Induction time (min)	1.38±0.49	1.3±0.47	0.53
Awakening time (min)	4.66±1.49	4.77±1.68	0.79
Discharge time (min)	41.03±8.38	32.83±5.97	*0.00

*statistically significant ($p<0.05$). SD- SD-standard deviation. Tests- Unpaired t test for first three variables and Fisher's Exact test for remaining variables.

***Table 2**. Comparison of adverse events.*

Parameters	Group I (n=29)	Group II (n=30)	P value	Parameters
Airway instrumentation [n(%)]	6 (20.6)	2 (6.6)	0.14	Airway instrumentation [n(%)]
Apnoea [n(%)]	0	0		Apnoea [n(%)]
Bradypnoea [n(%)]	1 (3.4)	0 (0)	0.49	Bradypnoea [n(%)]
Hypoxia [SpO2<95%]	0	0		Hypoxia [SpO2<95%]
Bradycardia [n(%)]	0 (0)	2 (6.6)	0.49	Bradycardia [n(%)]
Nausea or vomiting [n(%)]	0	0		

$p<0.05$ is statistically significant. Test- Fisher's Exact.

Discussion

Magnetic resonance imaging (MRI) of brain requires sedation to provide immobility, anxiolysis, and amnesia.[1,7] Deep sedation is always associated with upper airway obstruction.[8] All these airway related complications can be prevented by giving general anaesthesia (GA) with

secured airway, but it requires MRI compatible anaesthesia machine.[7,9]

Propofol provides uniform depth of sedation.[2,7] However it causes hypotension and upper airway collapsibility.[8] Hence addition of adjuvant drugs like midazolam, ketamine or dexmedetomidine have been recommended. In our study we used either midazolam or magnesium sulfate as adjuvants to propofol. Both regimes were found to be satisfactory for obtaining good quality MRI brain images. The need for airway interventions were not statistically significantly in both groups, but were less in group II.

Propofol-midazolam combination has synergistic action and hence provides short induction time and fast recovery.[2,3,10] Our results are in line with previous studies**.** Magnesium sulfate is successfully used as a sedative agent in some paediatric procedures and surgeries.[11] Its sedative and antiepileptic property is useful in epileptic patients as it reduces neuronal excitability and prevent convulsions.[12] Magnesium sulfate by acting as an inhibitor of acetycholine release, might be responsible for reduction of muscle spasm and pain in patients with cerebral palsy. This may be one of the reasons for reduction in intraoperative anaesthetic requirements.[13] However we did not find reduction in the number of additional bolus doses of propofol by prior administration of magnesium sulfate. This may be because we did not use infusion of magnesium sulfate for maintenance of sedation. But we successfully used the magnesium sulfate sedation for brain MRI in patients with epilepsy and cerebral palsy, with a comparable sedation profile to midazolam.

We assumed that the anaesthetic sparing properties of magnesium sulfate could reduce the dose and hence cardiorespiratory complications of propofol.[4,11] Premedication with $MgSO_4$ is associated with lower incidence of laryngospasm, bronchial hyperreactivity or airway obstruction.[4] Unlike benzodiazepines, at therapeutic doses magnesium sulfate does not cause respiratory depression or breath holding.[10,11,13] However benzodiazepines have relaxing effect on pharyngeal muscles causing airway obstruction. This may be the explanation for the higher incidence of airway manipulation in our group I population. Emergence agitation is known to occur after painful as well as pain-free radiological diagnostic procedures.[11] Magnesium sulfate was found to reduce the incidence of emergence agitation. Our results are in line with previous studies**.**[13,14,15] Lower incidence of emergence agitation and other airway related complications, along with good recovery profile may be the reason for early discharge time in our group II population. A paradoxical reaction to midazolam may be a possible cause for increased incidence of emergence agitation in our group I population.[16] . To date this is the first study where magnesium sulfate was successfully used along with propofol, as an alternative to midazolam for diagnostic MRI of brain in children having cerebral palsy and epilepsy. This study may promote for further studies in the future regarding the use of various dose regimens of Magnesium Sulfate.

We failed to monitor BP, electrocardiography and BIS monitoring during the procedure due to non availability of MRI compatible monitor.

Conclusion

Midazolam/Propofol and MgSO4/Propofol in combination provide satisfactory sedation for brain MRI in children. Lower need for airway interventions, lower incidence of emergence agitation and faster recovery time seen with MgSO4 favors the use of a sedation regime using MgSO4 in combination with Propofol.

References

1. Eldeek AM, Elfawal SM, Allam MG. Sedation in children undergoing magnetic resonance imaging comparative study between dexmedetomidine and ketamine. Egypt J Anaesth 2016;32:263-8.

2. Balasubramanian B, Malde AD, Kulkarni SB. A non-randomized controlled study of total intravenous anesthesia regimens for magnetic

resonance imaging studies in children. J Anaesthesiol Clin Pharmacol 2019;35:379-85

3. Akbulut UE, Kartal S, Dogan U, Akcali GE et al. Propofol with and without Midazolam for Diagnostic Upper Gastrointestinal Endoscopies in Children. Pediatr Gastroenterol HepatolNutr. 2019;22:217-224.

4. EizagaRebollar R, García Palacios MV, Morales Guerrero J, Torres LM. Magnesium sulfate in pediatric anesthesia: the Super Adjuvant. PaediatrAnaesth. 2017;27:480-489.

5. S. H. Kim, D. H. Kim, H. Kang et al. Estimation of teeth-to-vallecula distance for prediction of optimal oropharyngeal airway length in young children. Br. J. Anaesth.2011; 107:769–773.

6. Leila L Reduque, Susan T Verghese, Paediatric emergence delirium, *Continuing Education in Anaesthesia Critical Care & Pain*. 2013;13:39–41

7. Maddirala S, Theagrajan A. Non-operating room anaesthesia in children. Indian J Anaesth. 2019;63:754-762.

8. Mishima G, Sanuki T, Sato S, Kobayashi M, Kurata S, Ayuse T. Upper-airway collapsibility and compensatory responses under moderate sedation with ketamine, dexmedetomidine, and propofol in healthy volunteers. Physiol Rep. 2020;8:e14439.

9. Ucisik-Keser FE, Chi TL, Hamid Y et al. Impact of airway management strategies on magnetic resonance image quality. Br J Anaesth 2016;117: i97102.

10. Kang R, Shin YH, Gil NS et al. A comparison of the use of propofol alone and propofol with midazolam for pediatric magnetic resonance imaging sedation - a retrospective cohort study. BMC Anesthesiol. 2017;17:138.

11. Xie M, Li XK, Peng Y. Magnesium sulfate for postoperative complications in children undergoing tonsillectomies: A systematic review and meta-analysis. J. Evid. Based Med. 2017;10:16–25.

12. Tan WW, Chan DWS, Lee JH et al. Use of Magnesium Sulfate Infusion for the Management of Febrile Illness-Related Epilepsy Syndrome: A Case Series. Child Neurol Open. 2015;2:2329048X14550067

13. Rodríguez-Rubio L, Solis Garcia Del Pozo J, Nava E, Jordán J. Interaction between magnesium sulfate and neuromuscular blockers during the perioperative period. A systematic review and meta-analysis. J Clin Anesth. 2016 ;34:524-34.

14. Lee, Y.-J.; Kim, B.-Y.; Park, J.-H et al. The Effect of Intraoperative Magnesium Sulphate Infusion on Emergence Agitation after Ambulatory Ophthalmic Surgery in Children. *J. Clin. Med.* 2020; *9*: 4126.

15. Cavalcanti IL, Lima FLT, Silva MJS, Cruz Filho RA, Braga ELC and Verçosa N. et al. Use Profile of Magnesium Sulfate in Anesthesia in Brazil. Front Pharmacol. 2019;10:429.

16. Dave NM. Premedication and induction of anaesthesia in paediatric patients. Indian J Anaesth 2019;63:713-20.